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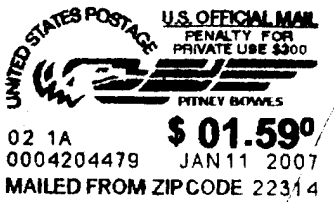

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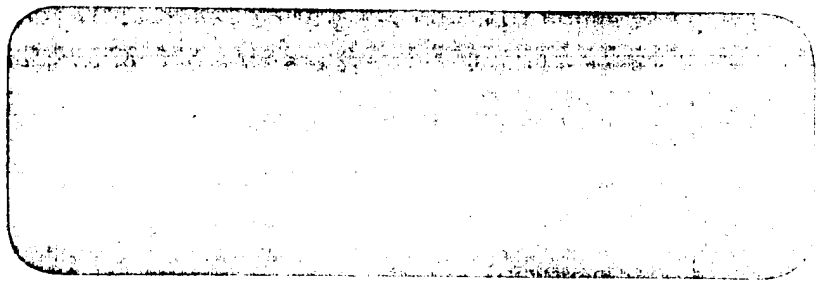

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OIPE IAP86
JAN 25 2007
PATENT & TRADEMARK OFFICE

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/777,010	02/11/2004	Carsten-Peter Carstens	25436/1344	3414

27495 7590 01/11/2007

PALMER & DODGE, LLP
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EXAMINER	
BURKHART, MICHAEL D	
ART UNIT	**PAPER NUMBER**
1633	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	01/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

OIPE JAN 25 2007 PATENT & TRADEMARK OFFICE

Office Action Summary	Application No.	Applicant(s)	
	10/777,010	CARSTENS, CARSTEN-PETER	
	Examiner	Art Unit	
	Michael D. Burkhart	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 45-61 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 45-61 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 2/04; 9/05.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Specification

The amendment filed 11/2/2006 is objected to under 35 U.S.C. 132(a) because it introduces new matter into the disclosure. 35 U.S.C. 132(a) states that no amendment shall introduce new matter into the disclosure of the invention. The added material which is not supported by the original disclosure is as follows: SEQ ID NOs 14-16. There is no support for the entirety of these sequences in the specification as filed (SEQ ID NOs 14 and 15 are 10 Kb, and SEQ ID NO 16 is 1.1. Kb). If they are the GenBank Accession Nos. referenced on pages 23 and 24 of the specification, in the context of the specification the Accession Nos. are used only to indicate where within the Accession Nos the specific primers in the PCR anneal, it is not even disclosed that the Accession Nos. were the actual PCR template (e.g. page 23, lines 19-26). Hence, the only support found for any sequences from these Accession Nos. is the inherent support that the PCR primers used in the specification anneal at specific regions in the Accession Nos. This does not provide support for entire Accession Nos., which, at best, appear to be what is contained in the Sequence Listing.

Applicant is required to cancel the new matter in the reply to this Office Action.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 50-52 and 59-61 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 50-52 and 59-61 recite tRNA sequences comprising sequences found between specific base pairs of Genbank Accession Nos. The specification provides no guidance on which, if any, of the SEQ ID NOs in the Sequence Listing corresponds to the Genbank Accession Nos. recited in the claims. Furthermore, because the content of Genbank entries can (and do) change over time due to corrections, it cannot be determined if the sequences represented by the SEQ ID NOs (if they are the recited Genbank Nos.) are the actual DNA sequences as they existed at the time of filing of the instant application (applicants claim priority to 1999). Therefore, it cannot be determined what the actual tRNA sequences must be in order to anticipate the claims, preventing a satisfactory search of the claims. Thus, the metes and bounds of the claimed subject matter are unclear, and a search of the prior art regarding these specific sequences cannot be performed.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 50-52 and 59-61 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the

relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The recitation of tRNA sequences comprising sequences of Genbank Accession Nos. in claims 50-52 and 59-61 is an attempt to incorporate essential, claimed subject matter by reference to prior art documents (i.e. the Genbank entries). A review of the disclosure as filed does not reveal these DNA sequences, thus there is no evidence applicants had possession of these specific DNA sequences. The incorporation of essential material in the specification by reference to an unpublished U.S. application, foreign application or patent, or to a publication is improper. See MPEP §608.01(p) (I). Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the Office. The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f).

The attempt to incorporate subject matter into this application by reference to the Genbank Accession Nos. recited in claims 50-52 and 59-61 is ineffective because the Accession Nos. are non-patent prior art documents (i.e. not a U.S. Patent or published U.S. application). The incorporation by reference will not be effective until correction is made to comply with 37 CFR 1.57(b), (c), or (d). If the incorporated material is relied upon to meet any outstanding objection, rejection, or other requirement imposed by the Office, the correction must be made within any time period set by the Office for responding to the objection, rejection, or other requirement for the incorporation to be effective. Compliance will not be held in abeyance with

respect to responding to the objection, rejection, or other requirement for the incorporation to be effective. In no case may the correction be made later than the close of prosecution as defined in 37 CFR 1.114(b), or abandonment of the application, whichever occurs earlier.
Any correction inserting material by amendment that was previously incorporated by reference must be accompanied by a statement that the material being inserted is the material incorporated by reference and the amendment contains no new matter. 37 CFR 1.57(f).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 45-48, 53-56, and 58 are rejected under 35 U.S.C. 103(a) as being unpatentable over Del Tito et al (cited in the IDS of 2/11/2004) in view of Nakamura et al, Zhang et al, Saier, Kawakami et al, Clouthier et al (see applicants' exhibits A-G in the response filed 9/26/2002 in parent application 09/492,590) and Sprinzl et al (Nuc. Acids Res., 1998).

Del Tito et al teach the construction and use of a plasmid, pRI952, which comprises an array of two tRNA genes (argU and IleX) encoding tRNAs specific for the rarely used codons AGG/AGA and AUA, respectively (e.g. page 7087, paragraph 2; Tables I and II). The authors teach that PRI952 was constructed by insertion of a PCR-amplified DNA comprising the gene (comprising the endogenous tRNA promoter) for ileX flanked by HindIII restriction sites into

pDC592, a pACYC184 derivative (i.e. low copy number plasmid comprising the *tet* promoter and chloramphenicol resistance gene, see description and diagram of pACYC184, GenBank accession number X06403) already possessing the argU gene (e.g. pages 7087, column 2, paragraph 2). Del Tito et al teach that coexpression of the two tRNA genes along with the gene encoding the heterologous polypeptide Mup^r IRS results in increased levels of active protein as compared to a control in which no additional tRNA genes are expressed or as compared to cells comprising a plasmid only expressing the ileX gene (e.g Table II). Del Tito et al teach that "...problems in expression can be avoided by a careful inspection of the coding sequence and inclusion of appropriate tRNA genes or necessary site-specific mutations." (page 7087, column 1, paragraph 2). The authors conclude that the co-expression of minor tRNAs such as ileX or argU can be utilized to overcome translational stresses due to the presence of rarely used codons within the coding sequence for a gene of interest (e.g. page 7091, column 1, paragraph 3). Del Tito et al teach the purification by reverse-phase HPLC of another heterologous polypeptide (i.e. the B/LeeHA antigen) produced by their system for compensating for the presence of rare codons in the coding sequence for the desired polypeptide (e.g. page 7088, column 1, paragraphs 3-4).

Del Tito et al do not explicitly teach the use of a vector comprising an array of the three tRNAs argU, ileY, and leuW.

Nakamura et al (Nucleic Acids Research, 1996, Vol. 24, pages 214-215; see the entire reference) provide codon usage data tabulated from the GenBank international DNA sequence databases for 4,805 species (e.g. prokaryotes, protozoa, fungi, animals and plants).

Zhang et al (Gene, 1991, pages 61-72, see the entire reference) detail low usage codons in species as diverse as E. coli, yeast, Drosophila and primates.

Saier, M. H. (FEBS, 1995, Vol. 362, pages 1-4; see the entire document) teaches the rare codon usage in several different species (e.g. R. capsulatus, R. speriodes, C. acetobutylicum, S. coelicular and E. coli).

Sprinzl et al (Nucleic Acids Research, 1998, Vol. 26, , pages 148-153); see the entire document) teach a compilation of 3,279 sequences of tRNA genes (including the *E. coli* argU, ileY, and leuW genes) including cellular and mitochondrial tRNAs from bacteria and phage, plants, yeasts and fungi, insects, amphibians and mammals, including rats, mice, cows and humans.

Kawakami et al (1993, Genetics, Vol. 135, pages 309-320; see the entire document) teach a rare Arg-tRNA-CCU in S. cerevisiae).

Clouthier et al (J. Bacteriology, 1998, Vol. 180, pages 840-845, see the entire document) teach a rare Arg-tRNA-AGA from S. enteritidis.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the vector construct taught by Del Tito et al for compensating for the presence of rarely used codons present in the gene encoding a protein of interest by interchanging and/or adding different tRNA genes corresponding to other rarely used codons in a given cell type, because Del Tito et al teach that it is within the skill of the art to carefully scrutinize the coding sequence of a protein, identify rarely used codons and compensate for the presence of such rarely codons by supplying in trans the tRNA corresponding to the identified rarely used codons from a vector expressing different tRNA genes, and because the rarely used codons and corresponding

genes were widely known in the art (i.e. the teachings of Nakamura et al, Zhang et al, Saier, Sprinzl et al, Kawakami et al and Clouthier et al). One would have been motivated to do so in order to meet the particular rare-codon requirements of a gene encoding a desired protein in combination with a given cell type, and thus receive the expected benefit of increasing its expression in the given cell type, as taught by Del Tito et al. Absent any evidence to the contrary, there would have been a reasonable expectation of success in utilizing any tRNA gene obtained from any cell type that was known in the art (i.e. ileY, proL, leuW, etc.) in the approach taught by Del Tito et al to increase the production of a desired protein that comprises rarely used codons.

Regarding the limitations of instant claims 46, 47, 55, and 56, these are matters of design choice in the preparation of the vector. Del Tito et al teach the insertion of the ileX gene, flanked by HindIII sites, into the pDC592 vector. Thus, the gene could have been inserted in either orientation relative to the argU gene. Such choices are dependent upon the method steps used to construct the vector, the sequence of the tRNA gene chosen, and the location of convenient restriction sites in the chosen vector. Applicants choice of an order of argU, ileY, and leuW appears arbitrary from a reading of the specification and imparts no discernable advantage to the vector. The same is true for the orientation of the ileY gene relative to the other tRNAs. Given that the basic concept that is the crucial element of the invention was already known in the art (i.e. providing tRNAs corresponding to rarely used codons from DNA constructs comprising the cognate tRNA genes), that applicants' invention differs only in the make-up of the DNA constructs that are used to express the tRNA genes, and that the means and materials for making the changes necessary to the constructs taught by Del Tito et al in order to

arrive at the claimed invention, it is the examiner's conclusion that there is no significant contribution from the instant application that was not already readily available from the prior art.

Claims 49 and 57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Del Tito et al, Nakamura et al, Zhang et al, Saier, Kawakami et al, Clouthier et al, and Sprinzl et al as applied to claims 45-48, 53-56, and 58 above, and further in view of Skerra et al (U.S. 5,849,576, 1998).

The teachings of el Tito et al, Nakamura et al, Zhang et al, Saier, Kawakami et al, Clouthier et al, and Sprinzl et al are as above and applied as before, except: Del Tito et al teach that the expression of tRNA genes has been shown to be deleterious to the host cell and that for this reason the ileX promoter was used to control expression of the ileX gene from low-copy number plasmids (page 7090, column 2, ¶ 3).

None of the above references teach the use of the *tet* promoter operably linked to the tRNA genes.

Skerra et al teach the use of the *tet* promoter to control expression of toxic genes in *E. coli* (see entire document, particularly the abstract and column 2, lines 49-55).

It would have been obvious to one of ordinary skill in the art at the time of the invention to use the *tet* promoter (and the regulable tetracycline expression system) described by Skerra et al with the vectors of Del Tito because Del Tito et al teach that the expression of tRNA genes in *E. coli* can have a negative effect on the host cell. Skerra et al teach that a system for the tightly controlled expression of target, toxic genes in *E. coli* was well known and widely used within the art for the expression of toxic genes in *E. coli*. One would have been motivated to do so in order

to receive the expected benefit of avoiding any potential toxic effects associated with the expression of the tRNA genes in *E. coli* during periods when expression of said tRNA genes was not required. Absent any evidence to the contrary, there would have been a reasonable expectation of success in utilizing the *tet* promoter expression system for the controlled expression of tRNA genes in *E. coli* for the purpose of expression of desired polypeptides whose coding sequence comprises a number of different, rarely used codons.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 54 and 58 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter. The nucleic acid is not recited as purified or isolated, and thus reads on the *E. coli* genome, a product of nature. According to the specification and claims, the *E. coli* genome contains all three of the tRNA genes specified in the claim.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael D. Burkhart whose telephone number is (571) 272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Michael D. Burkhart
Examiner
Art Unit 1633

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER

Notice of References Cited	Application/Control No.	Applicant(s)/Patent Under Reexamination	
	Examiner	Art Unit	Page of

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U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
	A	US-			
	B	US-			
	C	US-			
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	E	US-			
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FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
*	U	Saier, M., "Differential codon usage: a safeguard against inappropriate expression of specialized genes?" 1995, FEBS Lett., Vol. 362: pp. 1-4.
*	V	Kawakami, K. et al., "A Rare tRNA-Arg(CCU) That Regulates Ty1 Element Ribosomal Frameshifting Is Essential for Ty1 Retrotransposition in S. cerevisiae", 1993, Genetics, Vol. 135: pp. 309-320.
*	W	Clouthier, S. et al., "tRNA-Arg(fimU) and Expression of SEF14 and SEF21 in Salmonella enteritidis", 1998, J. Bacteriol., Vol. 180: pp. 1-13.
	X	

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

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OIPE IAF96 JAN 25 2007 PATENT & TRADEMARK OFFICE

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INFORMATION DISCLOSURE STATEMENT

Attorney Docket No.	Serial No.
25436/1344	10/777,010
Applicant(s):. Carstens	
Filing Date: February 11, 2004	Group: 1653

U.S. PATENT DOCUMENTS

Examiner Initial		Patent No.	Date	Name	Class	Subclass	Filing Date (if appropriate)

FOREIGN PATENT DOCUMENTS

Examiner Initial		Document No.	Publication Date	Country	Class	Subclass	Translation	
							YES	NO
MB	1.	EP0835938A2	April 15, 1998	EP	C12N	15/61		

OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, etc.)

MB	2.	Makrides, "Strategies for Achieving High-Level Expression of Genes in *Escherichia coli*", Microbiological Reviews (1996), V. 60, No. 3, Pages 512-538.
MB	3.	Copy of the European Examination Report.

EXAMINER /Michael Burkhart/	DATE CONSIDERED 01/03/2007

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

**Copies of references not provided at the time of this submission.

OIPE IAP96
JAN 25 2007
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Date of Deposit: February 11, 2004

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INFORMATION DISCLOSURE STATEMENT

Attorney Docket No.	Serial No.
25436/1344	10/777,011 ~~Not yet assigned~~

Applicant(s):. Carstens, Carsten-Peter

Filing Date: February 11, 2004 | Group: 1633 ~~Not yet assigned~~

U.S. PATENT DOCUMENTS

Examiner Initial		Patent No.	Date	Name	Class	Subclass	Filing Date (if appropriate)
MB		6,270,988	August 7, 2001	Brinkmann, et al.	435	69.1	

FOREIGN PATENT DOCUMENTS

Examiner Initial		Document No.	Date	Country	Class	Subclass	Translation	
							YES	NO

OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, etc.)

MB		Kane, J.F., "Effects of rare codon clusters on high-level expression of heterologous proteins in Escherichia cole", *Current Opinion in Biotechnology* 6:494-500 (1995);
MB		Bonekamp, et al, "Codon-defined ribosomal pausin in Escherichia coli detected by using the pyer attenuator to probe the coupling between transcription and translation", *Nucleic Acid Res* 13:4113-23 (1985);
MB		Deana, A., et al. "Silent Mutations in the Escherichia coli ompa leader peptide region strongly affect transcription and translation in vivo", *Nucleic Acids Res* 26:4778-4782 (1998);
MB		Rosenberg, A.H., et al., "Effects of consecutive AGG condons on translation in Escherichia coli, demonstrated with a versatile codon test system" J. Bacteriol 175:716-22 (1993);
MB		Goldman, E., et al., "Consecutive low usage leucine codons block translation only when near the 5' end of a message in Escherichia Coli" J. Mol. Biol. 245:467-73(1995);
MB		Degryse, E., "Influence of the second and third codon on the expression of recombinant hirudin in E. Coli" FEBS Lett, 269:244-6 (1990);
MB		Spanjaard, R.A., et al., "Frameshirt suppression at tandem AGA and AGG Condons by cloned tRNA genes: assigning a codon to argu tRNA and T4 tRNA (Arg)", *Nucleic Acids Res.* 18:5031-6 (1990);
MB		Kane, J.F., et al, "Novel in frame two codon translationalhop during synthesis of bovine placental lacotogen in a recombinant strain of Escherichia coli", *Nucleic Acids Res.* 20:6707-12 (1992);
MB		Calderone, T.L., et al., "High-level misincorporation of lysine for arginine at AGA codons in a fusion protein expressed in Escherichia coli", J. Mol. Biol 262: 407-12 (1996);
MB		Forman, M.D., et al "High level, context dependent misincorporation of lysine for arginine in Saccharomyces cerevisiaw a 1 homodomain expressed in Escherichia coli", *Protein Sci* 7:500-3 (1998);
MB		Brinkman, et al. "High level expression of recombinant genes in Escherichia Coli is dependent on the availability of the dna Y gene product", Gene 85:109-14 (1989);

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Express Mail label No.: EV242754784US
Date of Deposit: February 11, 2004

USPTO Form 1449 U.S. Department of Commerce
Patent and Trademark Office

INFORMATION DISCLOSURE STATEMENT

Attorney Docket No.	Serial No.
25436/1344	10/777,010 ~~Not yet assigned~~
Applicant(s):. Carstens, Carsten-Peter	
Filing Date: February 11, 2004	Group: 1633 ~~Not yet assigned~~

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FOREIGN PATENT DOCUMENTS

Examiner Initial		Document No.	Date	Country	Class	Subclass	Translation	
							YES	NO

OTHER DOCUMENTS (including Author, Title, Date, Pertinent Pages, etc.)

MB		Hua, et al, "Enhancement of Expression of human granulocyte-macrophage colony stimulating factor by argu gene product in escherichia coli" *Biochem Mol. Biol. Int.* 32:537-43 (1994);
MB		Chen, et al., "Role of the AGA/AGG codons, the rarest codons in global gene expression in Escherichia coli" *Genes Dev* 8:2641-52 (1994);
MB		Garcia, et al., "The argU Gene product enhances expression of the recombinant human interferon in Escheria coli" Ann N.Y. Acad Sci 782:79-86;
MB		Kim, et al., "Overexpression of archael proteins in Escherichia coli" *Biotech. Lett* 20:207-210 (1998);
MB		Rojiani, et al. "Relationship between protein synthesis and concentrations of charged and uncharged tRNA in Escheria Coli" *Proc. Nat. Acad. Sci U.S.A.* 87:1511-1515 (1990);
MB		Sharp, et al., "Codon usage in regulatory genes in Escherichia coli does not reflect selevtion for rare codons" *Nucleic Acids Res.* 14:7737-7749 (1986); and
MB		Del Tito, Jr., et al. "Effects of a Minor Isoleucy 1 tRNA on Heterologous Protein Translation in Escherichia coli.", Journal of Bacteriology, December 1995, Vol. 177, No.: 24 pages 7086-7091.

EXAMINER /Michael Burkhart/	DATE CONSIDERED 01/03/2007

*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

**Copies of references not provided at the time of this submission.

Notice of References Cited

Application/Control No.	Applicant(s)/Patent Under Reexamination	
10/777,010	CARSTENS, CARSTEN-PETER	
Examiner	Art Unit	Page 1 of 1
Michael D. Burkhart	1633	

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U.S. PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Name	Classification
*	A	US-5,849,576	12-1998	Skerra et al.	435/320.1
	B	US-			
	C	US-			
	D	US-			
	E	US-			
	F	US-			
	G	US-			
	H	US-			
	I	US-			
	J	US-			
	K	US-			
	L	US-			
	M	US-			

FOREIGN PATENT DOCUMENTS

*		Document Number Country Code-Number-Kind Code	Date MM-YYYY	Country	Name	Classification
	N					
	O					
	P					
	Q					
	R					
	S					
	T					

NON-PATENT DOCUMENTS

*		Include as applicable: Author, Title Date, Publisher, Edition or Volume, Pertinent Pages)
	U	Sprinzl, M. et al., "Compilation of tRNA sequences and sequences of tRNA genes", Jan. 1998, Nuc. Acids Res., Vol. 26: pp. 148-153.
	V	pACYC184 description and map: Fermentas technical information web page, updated 10/8/2006, www.fermentas.com/techinfo/nucleicacids/mappacyc184.htm, 2 pages.
*	W	Nakamura, Y. et al "Codon usage tabulated from the international DNA sequence databases", 1996, Nuc. Acids Res., Vol. 24: pp. 214-215.
*	X	Zhang, S. et al., "Low-usage codons in Escherichia coli, yeast, fruit fly and primates", 1991, Gene, Vol. 105: pp. 61-72.

*A copy of this reference is not being furnished with this Office action. (See MPEP § 707.05(a).)
Dates in MM-YYYY format are publication dates. Classifications may be US or foreign.

pACYC184: description & restriction map

Related Documents:

GenBank/EMBL accession number X06403.

Restriction sites

Sequence

Not available from Fermentas

The 4245 bp plasmid, pACYC184, is compatible with pMB1- or ColE1-related plasmids and can therefore be used together with a pMB1- or ColE1-derivative within the same cell. pACYC184 contains: (**1**) the replicon *rep* responsible for the replication of plasmid (source - plasmid p15A); (**2**) *tet* gene, encoding tetracycline resistance protein (source - plasmid pSC101); (**3**) *cat* gene, coding for chloramphenicol acetyl transferase that confers resistance to chloramphenicol (source - transposon Tn9).

The circular sequence is numbered such that 1 is the first G of the unique EcoRI site GAATTC and the count increases first through the 5'-terminal part of *cat* gene, the p15A material, the *tet* gene and finally through the 3'-terminal part of *cat* gene. The map shows enzymes that cut pACYC184 DNA once. Enzymes produced by Fermentas are shown in blue. The coordinates refer to the position of first nucleotide in each recognition sequence.

The exact position of genetic elements is shown on the map (termination codons included). The indicated *rep* region is sufficient to promote replication. DNA replication initiates at position 846 (+/- 1) and proceeds in the direction indicated.

Derivatives of p15A are normally present in a somewhat lower copy number than pMB1 derivatives and cannot be amplified to the same extent as pMB1 derivatives. Due to the presence of the *cat* gene on pACYC184, amplification of this plasmid should be performed using spectinomycin.

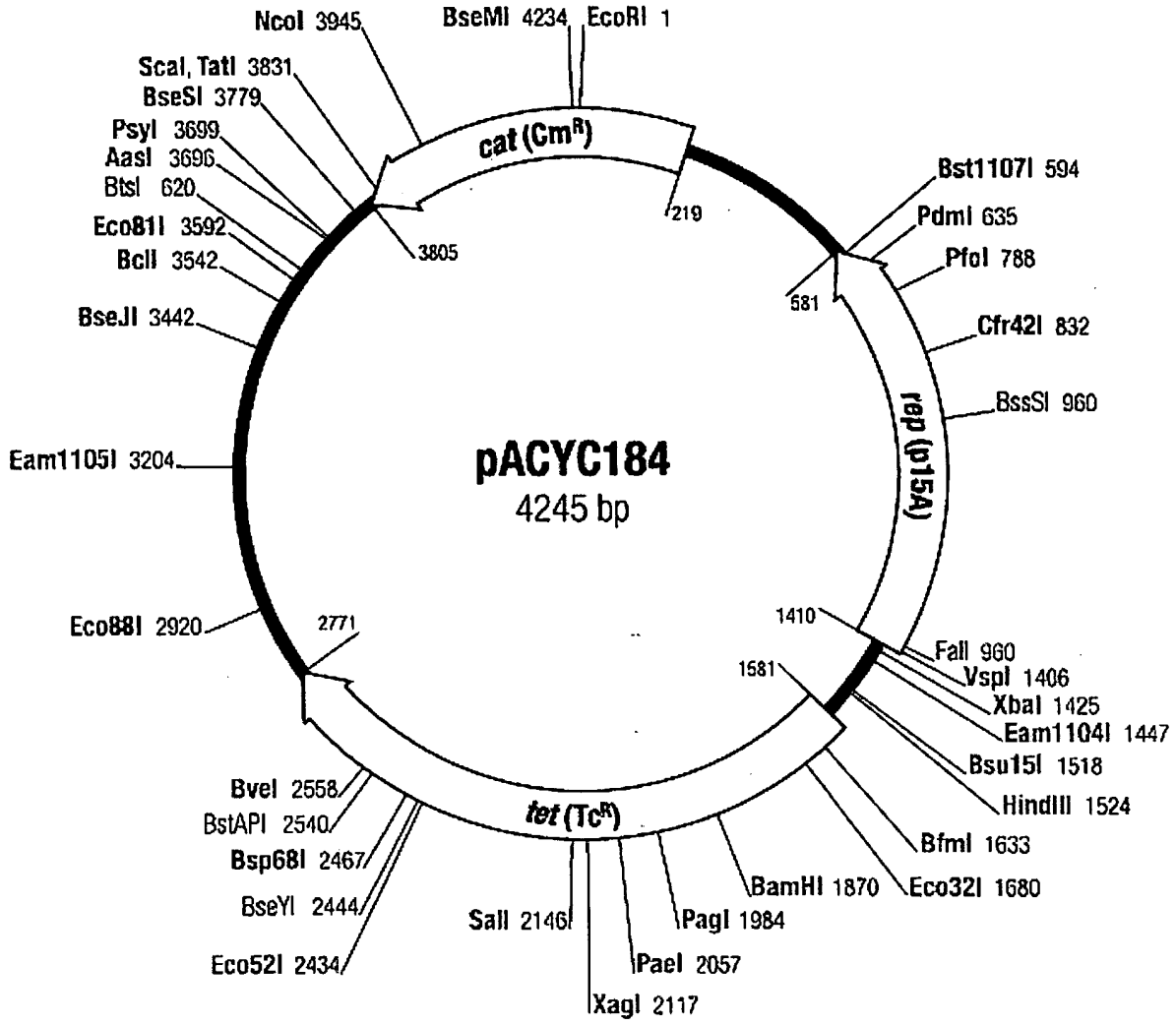
References

1. Chang, A.C.Y. and Cohen, S.N., Construction and characterization of amplifiable multicopy DNA cloning vehicles derived from the P15A cryptic miniplasmid, J. Bacteriol., 134, 1141-1156, 1978.

2. Rose, R.E., The nucleotide sequence of pACYC184, Nucleic Acids Res., 16, 355, 1988

Enzymes which cut pACYC184 DNA once:
AasI 3696, **BamHI** 1870, **BclI** 3542, **BfmI** 1633, **BseJI** 3442, **BseMI** 4234, **BseSI** 3779,

BseYI 2444, **Bsp68I** 2467, **BssSI** 960, **Bst1107I** 594, **BstAPI** 2540, **Bsu15I** 1518, **BtsI** 3620, **BveI** 2558, **Cfr42I** 832, **Eam1104I** 1447, **Eam1105I** 3204, **Eco32I** 1680, **Eco52I** 2434, **Eco81I** 3592, **Eco88I** 2920, **EcoRI** 1, **FalI** 1395, **HindIII** 1524, **NcoI** 3945, **PaeI** 2057, **PagI** 1984, **PdmI** 635, **PfoI** 788, **PsyI** 3699, **SalI** 2146, **ScaI** 3831, **TatI** 3831, **VspI** 1406, **XagI** 2117, **XbaI** 1425.



Updated November 08, 2006 14:24

148–153 Nucleic Acids Research, 1998, Vol. 26, No. 1 © 1998 Oxford University Press

Compilation of tRNA sequences and sequences of tRNA genes

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Received September 16, 1997; Revised and Accepted October 6, 1997

ABSTRACT

Sequences of 3279 sequences of tRNA genes and tRNAs published up to December 1996 are included in the compilation. Alignment of the sequences, which is most compatible with the tRNA phylogeny and known three-dimensional structures of tRNA, is used. Sequences and references are available under http://www.uni-bayreuth.de/departments/biochemie/trna/

INTRODUCTION

The 1997 compilation contains 3279 sequences of tRNAs and tRNA genes. The last edition which appeared two years ago (1) was supplemented by 579 new sequences covering the literature up to December 1995. The sequences of tRNA mutants and of tRNAs originating from transformed or differentiated cells were not considered.

The tRNAs included in the compilation are listed in Table 1. Each tRNA or tRNA gene is specified by the (abbreviated) name of the organism from which it was isolated and a four digit code: the first three digits identify the organism, the last digit specifies the particular isoacceptor. The amino acid specificity of the tRNA is indicated by a one-letter amino acid code. The tRNAs coding for selenocysteine were annotated with the letter Z. Initiator tRNAs are annotated with the letter X.

The references are restricted to the first publication of the complete sequence unless additional information (e.g., base modification, corrections, etc.) was later obtained. In such cases additional references were added.

In order to facilitate a computer analysis an alignment is used which is most compatible with the tRNA phylogeny and known three-dimensional structures of tRNA. The corresponding numbering system is shown in Figure 1.

As was the case in the previous edition (1), this publication does not contain a sequence printout. Instead, the sequences, references and footnotes of tRNAs and tRNA genes listed in Table 1 are deposited in the European Bioinformatics Institute (EBI) Data Library. In addition, a World Wide Web page has been established and is available under http://www.uni-bayreuth.de/departments/biochemie/trna/ . The present publication should be quoted as a reference for the electronically accessible data.

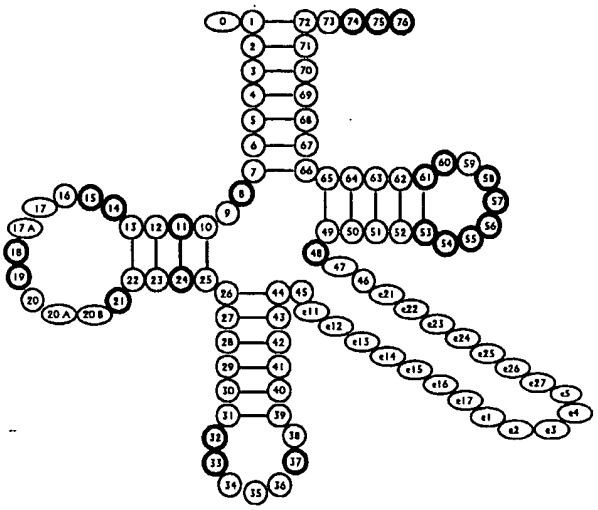

Figure 1. Numbering of nucleotides in tRNAs. Circles represent nucleotides which are always present; the ovals, nucleotides which are not present in each structure: these are nucleotides before the position 1 on the 5′-end, before and after the two invariant GMP residues 18 and 19 in the D-loop, and the nucleotides in the variable loop. The nucleotide to be added at a given site is indicated by the number of the preceeding nucleotide followed by a colon and a letter in alphabetical order. The nucleotides in the variable stem have the prefix 'e' and are located between position 45 and 46 obeying the base-pairing rules. The nucleotides in the 5′-strand and the 3′-strand are numbered by e11, e12, e13, ... and e21, e22, e23, ..., respectively; the second digit identifies the base-pair. In the case of a long variable region, the loop can be formed by up to 5 nt: e1, e2, e3, e4 and e5. Positions, in which invariant nucleotides usually occur are indicated by a thick line.

Researchers who wish to perform an advanced search for tRNA sequences according to several criteria, e.g., anticodon, amino acid specificity, modified nucleoside, or wish to print the requested sequence in the form of Table 2 or cloverleaf format (Fig. 1) can obtain appropriate software on diskette. Please contact M. Sprinzl, Laboratorium für Biochemie, Universität Bayreuth, D-95440 Bayreuth, Germany, Fax: +49 921 552432, Email: Mathias.Sprinzl@uni-bayreuth.de.

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Table 1. List of tRNA sequences and sequences of tRNA genes included in the compilation

PART ONE: Sequences of tRNA genes

Source	Code	tRNA genes
VIRUSES	000-029	
MYCOBACTERIOPH. L5	020	NQW
PHAGE PHI C31	031	
PHAGE T4	022	GILPQRST
PHAGE T5	026	ACDEFGHIIKLMNPQSSTVWXY
ARCHAEBACTERIA	030-109	
ARCHAEGLOBUS FULG.	034	A
HALOBACTERIUM CUT.	038	AC
HALOBACTERIUM HAL.	042	A
HALOBACTERIUM MAR.	044	LS
HALOBACTERIUM MED.	046	W
HALOFERAX VOLCANII	050	CW
METHANOBAC.FORMI.	058	A
METHANOBAC.THERM.	062	A
METHANOCOCCUS JAN.	065	AACDEFGGHIILLLKMMNQPPRRRSSSTTVVVWXY
METHANOCOC.VANI.	066	ADEFHIKLNPQRTTVY
METHANOTHRIX SOEH.	067	A
METHANOTHERM. FER.	068	ADEHIKLMNPST
RUMINOBACTER AMYLO	070	E
METHANOCOC.VOLTAE	074	DKPTY
METHANOPYRUS KAND.	076	KLQS
METHANOSPIR. HUNG.	078	A
SULFOLOBUS SOLFA.	086	FGILSVX
THERMOPLASMA ACID.	090	M
THERMOCOCCUS CELER.	094	APT
THERMOFIL. PENDENS	096	GM
THERMOPROT. TENAX	098	AALLX
EUBACTERIA	110-239	
BARTONELLA BACIL.	110	IX
BARTONELLA ELIZAB.	111	AI
BARTONELLA HENSELA.	112	I
BARTONELLA QUINT.	113	AI
MYCOPLASMA CAPRIC.	114	ACDEFGHIIKKLLMNPQRRSSTTVWWXY
MYCOPLASMA GEN.	115	ACDEFGGHIIIKKLLMMNPQRRSSSSTTTWWY
MYCOPLASMA MYCOID.	118	ADEFGIMNPRRSTVX
MYCOPLASMA PNEU.	120	ACDEEGGHIIKKLLLMNPQRRRSSSSTTTVWWXYY
MYCOPLASMA PG50	122	KL
ACHOLEPLASMA LAID.	123	AACDEFGHIIKKLLLMMNQRSSTVW
SPIROPLASMA CITRI.	125	SWW
SPIROPLASMA MELIF.	126	ACDFIMPRSX
BORRELIA BURGDORF.	128	AI
STREPTOMYCES GRIS.	130	S
STREPTOMYCES COEL.	131	L
STREPTOMYCES RIM.	134	EQQXX
STREPTOMYCES LIV.	135	CDEEEGGKNNQQRSVVY
STREPTOMYCES AMBO.	136	P
CHLOSTRIDIUM PERFR.	139	S
MYCOBACT. TUBERC.	140	PV
KLEBSIELLA AEROGE.	141	N
AGROBACTER. TUME.	142	R
CLOSTRIDIUM THERM.	143	Z
DESULFOMICR. BACU.	144	Z
CLOSTRIDIUM ACETO.	145	T
PLESIOMONAS SHIGE.	146	B
ENTEROCOCCUS HIRAE	147	A
STAPHYLOCOC. AURE.	148	ACDDFGGGGHIKLLLMPQRSSTTVVWXY
LACTOBAC. BULG.	150	DEGNPRSV
LACTOBAC.DELBRUEC.	152	S
LACTOCOCCUS LACTIS	153	AAAEFGHNSX
BACILLUS SUBTILIS	154	AAAACDEFFGGGHHIIIKKLLLLLLLMMNNPQRSSSTTTVWXXY
BACILLUS CIRCULANS	156	P
BACILLUS SP. PS3	157	DENSV
THERMUS THERMOPHI.	158	GGTTY
THERMOTOGA MARIT.	159	MMTWY
RHODOTHERMUS MAR.	160	AI
THIOBACILLUS FERRO	162	AI
STIGMATELLA AURANT.	163	GTTY
E.COLI	166	AACDEFGGGHIIIKLLLLLMNPPPQQRRRRRSSSSTTTTTVVVWXXYYZ
SALMONELLA TYPHI.	170	HLPRR
AZOSPIRILLUM LIPO.	172	KTV
TRICHODESMIUM SPEC	173	AI
PHOTOBACT. PHOSPH.	174	HP
PHOTOBAC. LEIOGNA.	175	LM
AEROMONAS HYDROPH.	178	AEHILPR
PSEUDOMONAS AER.	182	AGTTY
PSEUDOMONAS FLUOR.	184	AI
CAMPYLOBAC.JEJUNI	186	AI
RICKETTSIA PROW.	187	GWY
CAULOBACTER CRES.	189	AI
BRUCELLA SUIS	190	AI
BRUCELLA MELLITENS.	191	AI
BRUCELLA ABORTUS	192	AAII
AZORHIZOBIUM CAUL.	193	G
RHIZOBIUM MELILOTI.	194	L
AZOARCUS SP.BH72	195	IL
OCHROBACTRUM ANTH.	196	AI
BORDETELLA PERTUS.	198	L
HAEMOPHILUS INFLU.	200	AAAACDDDEFGGGHIIIKKKKLLLLLLMMMNNPQQRRRRSSSSTTVVWY
ANACYSTIS NIDULANS	210	AI
SYNECHOCYSTIS SP.	214	AACDFGGGHIIIHKKLLLLLNPPPQRRRRSSSSTTTVVWWXXY
SYNECHOCOCCUS SP.	215	L
CYANOPHORA PARAD.	218	AEGHILRS
PYLAIELLA LITTORA.	222	AI
STREPTOCOCCUS PN.	224	A
STREPTOCOCCUS SAL.	225	A
ORGANELLES		
CHLOROPLASTS	240-359	
CYANOPHORA PARAD.	240	AI
PYLAIELLA LITTORA.	241	AI
CHLAMYDOMONAS REIN	244	ACDEGHMRRTW
CHLAMYDOMO. MOEWU.	246	T
CHLORELLA ELLIPSO.	248	AIRS
LYCOPERSICON ESCU.	249	DLY
CUCUMIS SATIVUS	250	E
ASTASIA LONGA	251	ACDGIKLMPQRSSTV
EUGLENA GRACILIS	252	AACDEFGGHIIIKLLLMNPQRRSSTVWXXY
CRYPTOMONAS SPEC.	254	AIR
SPIROGYRA MAXIMA	255	I
ANTITHAMNION SP.	257	AI
CYANIDIUM CALDAR.	258	AIK
OLISTHODISCUS LUT.	259	AI
MARCHANTIA POLYM.	260	ACDEFGGHIIIKLLLMNPPQRRRSSSTTVVWXY
CUSCUTA REFLEXA	261	AHILMV
COLEOCHAETE ORBIC.	262	AI
HORDEUM VULGARE	264	GGMSTVX
TRITICUM AESTIVUM	268	CDEGGMPRSTWXY
ORYZA SATIVA	270	ACCDEFGGHIIILLLMMNPQRRSSSTTVVWY
ZEA MAYS	272	AACDEFGGHHIIKLLLLMNPQRRSSSSSTTTVVVWXXY
EPIFAGUS VIRGINIA.	274	LNR
ARABIDOPSIS THAL.	276	IMP
ALLIUM PORRUM	278	R
BRASSICA OLERACEA	280	L
GLYCINE MAX	284	AIMV
MEDICAGO SATIVA	288	H
NICOTIANA TABACUM	292	ACDEFGGHIIIKLLLMNPQRRSSSTTVVWXY
NICOTIANA DEBNEYI	296	H
OENOTHERA SP.	300	PW
DAUCUS CAROTA	301	V
GOSSYPIUM HIRSUTUM	302	H
PELARGONIUM ZONALE	304	R
PENNISETUM AMERICA	308	I
PETUNIA HYBRIDA	312	H
PHASEOLUS VULGARIS	316	H
HELIANTHUS ANNUUS	317	HNY
PISUM SATIVUM	320	DEGHKLNPRRSTVWXY
PINUS THUNBERGII	322	ACDEFGGHIIIKLLLMNPPQRRRSSSTTVVWXY
PINUS CONTORTA	323	HK
SINAPIS ALBA	324	HKQSV
SPINACIA OLERACEA	328	ACDEHIILMRSSTTVY
SPIRODELA OLIGORH.	332	NRR
VICIA FABA	336	EFHLLTY
SORGHUM BICOLOR	340	L
MITOCHONDRIA	360-599	
SINGLE CELL ORGANISMS AND FUNGI	360-419	
PROTOTHECA WICKER.	360	ACDEFGGHIIIKLLMNPQRRSSTVWXY
PYLAIELLA LITTOR.	361	KPY
CHONDRUS CRISPUS	362	ACEGGHIKLLMNPQRRSVWXY
PLATYMONAS SUBCORD.	363	KNPVY
CHLAMYDOMO. REINH.	364	MQW
ODONTELLA SINENSIS	365	AACDEFGGHIIIKLLNPPQRRSSTVWXY
PLASMODIUM FALCIP.	366	CDEGGHKLPQSSWXY
TRYPANOSOMA BRUCEI	368	AA
LEPTOMONAS COLLO.	369	H

Table 1. *continued*

PARAMECIUM PRIM.	372	XY
PARAMECIUM TETRA.	376	WY
PARAMECIUM AURELIA	377	FWY
TETRAHYMENA PYRIF.	380	EFHLWX
TETRAHYMENA THERM.	384	LXY
ASPERGILLUS FUMI.	387	EMMTV
ASPERGILLUS NIDUL.	388	ACCDEFGGHIKLLMMNPQRSSTVWXY
NEUROSPORA CRASSA	392	ACMR
PODOSPORA ANSERINA	396	DMNSVW
PODOSPORA CURVICOL	397	N
SACCHAROMYCES CER.	400	AACDEFGHIKLMNPQRRSSTTVVWXYY
SACCHAROMYCES EXI.	401	MP
PICHIA PUPERI	402	LMM
WILLIOPSIS MRAKII	403	KLMPQSV
SCHIZOSACCHA.POM.	404	GHLPQ
KLUYVEROMYCES LAC.	405	CKLQ
CANDIDA PARAPSILO.	406	CEFGHIKLNPRRTVWY
HANSENULA WINGEI	407	ACCDEFGHIKLLLMMMMNPQRRRSSTVVWY
TORULOPSIS GLAB.	408	ACDEFGHIKLMNPQRSSTTVWXY
WILLIOPSIS SUAVE	409	M
PICHIA JADINII	410	M
TRICHOPHYTON MENT.	409	AFLMMTV
TRICHOPHYTON RUBR.	412	DGHKMQRWY
PENICILLIUM CHRYS.	413	NRY
ASCOBOLUS IMMERSUS	415	NNQ
PLANTS	420-459	
ARABIDOPSIS THAL.	424	EMQSSY
GLYCINE MAX	428	EMX
SOLANUM LYCOPERS.	430	C
SOLANUM TUBEROSUM	431	X
LUPINUS LUTEUS	432	GINX
BRASSICA NAPUS	434	K
OENOTHERA SP.	436	CFGHILNPSSSWXY
PHASEOLUS VULGARIS	440	NSY
HELIANTHUS ANNUUS	441	CEGHIKMNPQVWX
TRITICUM AESTIVUM	444	CDEFKNPQQSSSWXYYY
ORYZA SATIVA	446	FHNPRSW
ZEA MAYS	448	CDEHKMMPSSWXY
MARCHANTIA POLYM.	450	ACDEFGGHIKLLLMMNPQRRRSSTVWY
LARIX	452	HH
ANIMALS	460-599	
FASCIOLA HEPATICA	462	ADIKNPSW
ASCARIS SUUM	464	ACDEFGHIKLLNPQRSSTVWXY
CAENORHABDI.ELEG.	468	ACDEFGHIKLLNPQRSSTVWXY
MYTILUS EDULIS	470	ACDEFGHIKLLMMNPQRSSTVWY
ARTEMIA SP.	472	EFS
LOCUSTA MIGRATORIA	476	ACDDEFGGHIKKLLLLNPPQRSSTTVWXY
PSEUDOREGMA BAMBU.	477	L
METRIDIUM SENILE	478	X
NEPHILA CLAVIPES	479	AAAA
AEDES ALBOPICTUS	480	AEFGLNRSV
LOLIGO BLEEKERI	481	KKKKK
APIS MELLIFERA	482	ACDDEFGHIKLLMPQRSSVWY
DAPHNIA PULEX	483	IQVWXY
DROSOPHILA MELANO.	484	ACCDDEFGGHIKKLLLQRSSTVWWXYY
DROSOPHILA YAKUBA	488	ACDEFGHIKLLNPQRSSTVWXY
DROSOPHILA VIRILIS	496	IQX
CHORISTONEURA FUM.	497	L
PISASTER OCHRACEUS	498	ACDEGLLNPQTVWXY
PROTOPTERUS DOLLOI	499	ACDEFGHIKLLMNPQRSTVWY
ASTERINA PECTINI.	500	ACDGHLLMNPQSSVWY
CERATITIS CAPITATA	501	AEFNRS
ASTERIAS FORBESII	502	ACDGLLNVWXY
CYPRINUS CARPIO	503	ACDEFGHIKKLLNPQRSSTVWXY
PARACENTROTUS LIV.	504	ACDEFFGHIKLLNPQRSSTVWXY
ANOPHELES QUADRIM.	505	ACDEFGHIKLLNPQRSSTVWXY
RAINBOW TROUT	506	FPT
ANAS PLATYRHYNCOS	507	ACDEFKLNSWY
STRONGYLOCEN.PURP.	508	ACDEFGHIKLLNPQRSSTVWXY
ACIPENSER TRANSM.	509	PT
GADUS MORHUA	510	ACDEFGHIKLLMNQRSSTVWY
ACANTHAMOEBA CAST.	511	ADEIKLMPQX
XENOPUS LAEVIS	512	ACDEFFGHIKLLNPQRSSTVWXY
ALLIGATOR MISSIS.	513	ACNWY
CROCODYLUS POROSUS	514	ACNWY
CARETTA CARETTA	515	ACNWY
RANA CATESBEIANA	516	ACFILNPQTWXY
MALACLEMYS TERRA.	517	ACNWY
SPHENODON PUNCTAT.	518	ACNY
EPICRATES SUBFLA.	519	ACEN
CEPHALORHYN.COM.	520	FPT
CROSSOSTOMA LACUS.	521	ACDEFGHIKLLNPQRSSTVWXY
CHICKEN	522	ACDEFGHIKLLMNPQRSSTVWY
DIDELPHIS VIRGINI.	523	DPT
ODOCOILEUS HEMIO.	524	PT
DICEROS BICORNIS	525	FP
MARMOSA SP.	526	DPT
PHILANDER SP.	527	D
RAT	528	ACCDDEFGHIKKLLNNNPPQQRSSSTTVWWXXY
METACHIRUS SP.	529	D
PHALANGER SP.	530	D
CNEDIMOPHORUS UNI.	531	EPT
MOUSE	532	ACDEFGHIKLLNPQRSSTVWXY
CERVUS NIPPON	533	PT
BALAENOPTERA PHYS.	534	ACDEFGHIKLLPQRTVWXY
BALAENOPTERA MUSC.	535	ACDEFGHIKLLNPQRSTVWXY
BOVINE	536	ACDEFGHIKLLNPQRSSTVWXY
HALICHOERUS GRYPUS	537	ACDEFGLNPQRRSTVWXY
PHOCA VITULINA	538	ACDEFGHIKLLNPQRSTVWXY
GADUS MORHUA	539	DEIPQST
LEPIDOSIREN PARAD.	542	V
RHINOCEROS UNICORN	544	ACDEFGHIKLLMNPQRTVWY
SCELOPORUS OCCID.	545	HILLMMVW
STRUTHIO CAMELUS	550	HILMRW
ERINACEUS EUROP.	555	ACDEFGHIKLMNPQRTVY
MACACA ASSAMENSES	556	HLS
MACACA NIGRA	557	HL
MACACA SILENUS	558	HL
MACACA THIBETANA	559	HL
GREEN MONKEY	560	F
SIAMANG	561	ACDEIKNWXY
MACACA FUSCATA	562	HLS
MACACA MULATTA	563	HLS
MACACA FASCICULA.	564	HLS
MACACA SYLVANUS	565	HLS
SAIMIRI SCIUREUS	566	HLS
PAPIO HAMADRYAS	567	HL
TARSIUS SYRICHTA	568	HLS
LEMUR CATTA	570	HLS
CHIMPANZEE	572	ACDEEFGHIKLLMNPQRSTVWXY
PYGMY CHIMPANZEE	573	ACDEIKNWXY
GIBBON	576	HLS
GORILLA	580	ACDEEGHIIKLMNPQRSTVWXY
ORANG UTAN	584	ACDEEFGHIKLLLMNPRSSTVWXY
HUMAN	588	AACCDEEFGHIKLLLMMNPQRRSSTVWX\
AEPYCEROS MELAMPUS	590	FV
BOSELAPHUS TRAGOC.	591	FV
CEPHALOPHUS MAXW.	592	FV
DAMALISCUS DORCAS	593	FV
GAZELLA THOMSONI	594	FV
KOBUS ELLIPSIPRYM.	595	FV
MADOQUA KIRKI	596	FV
ORYX GAZELLA	597	FV
TRAGELAPHUS IMBER.	598	FV
EUKARYOTIC CYTOPLASM	600-999	
SINGLE CELL ORGANISMS AND FUNGI	600-669	
PLASMODIUM FALSI.	603	AILMNRRTV
TRYPANOSOMA BRUCEI	605	KKKNNQQRRRTVVY
TETRAHYMENA PYRIF.	606	NQS
LEISHMANIA TARENT.	609	GIKLQRRTVW
DICTYOSTELIUM DIS.	616	AEEHKKLMNQRRSSSTTVVWWY
PHYSARUM POLYCEPH.	618	X
NEUROSPORA CRASSA	620	FLR
CANDIDA ALBICANS	621	LSS
PHYTOPHTHORA PAR.	622	D
PODOSPORA ANSERINA	624	SS
SACCHAROMYCES CER.	628	AAACDDEEEFFFFGGHIIKKKLLLMMNPI QQQRRRSSSSSTTTVVVWWWXXYY
SCHIZOSACCHA.POM	632	ADEEFHIKRRSSSVXX
CANDIDA CYLINDRA.	637	S
PLANTS	670-749	
CHLAMYDIA TRACHOM.	672	TW
ARABIDOPSIS THAL.	674	APSSSSSSVWWXYYYY
GLYCINE MAX	690	DMX
PHASEOLUS VULGARIS	698	LPP
NICOTIANA RUSTICA	706	SSSSSSSYY
PETUNIA SP.	710	N
HELIANTHUS ANNUUS	712	L
SORGHUM BICOLOR	714	G
ORYZA SATIVA	718	G
TRITICUM AESTIVUM	720	YYYYY
TRITICUM VULGARE	724	S
SOYBEAN	730	C
ANIMALS	750-999	
CAENORHABDI. ELEG.	756	AAADEEGGHIKKKLLLLLLNPPP QQRRRRRSSTTVVVWXYZ
BOMBYX MORI	768	AAEGK
DROSOPHILA MELANO.	774	ADEEEFGGHIKKLLMNPRRSSTVVXYZ
DROSOPHILA SIMUL.	780	S
SQUID	785	K
XENOPUS LAEVIS	792	AFKLNVXXYYYZ
PODOCORYNE CARNEA	793	CFGSS
CHICKEN	804	AADDFKPPWZ
MOUSE	810	ACCDEGHIKKLPPXZ

Table 1. *continued*

RAT	916	DDEEEEEEEEEPQGKLLLPPQQQQQQ
BOVINE	928	SZ
HUMAN	999	AEEGGGKKLLMNNPPQQQRR SSSSSTTTVVVVVVVVXXYY

PART TWO: tRNA Sequences

Source	Code	tRNA
VIRUSES	000-029	
AVIAN ONCO.-VIRUS	010	M
CHICKEN ASV/AMV/RS	014	W
MOUSE M-MULV	018	PP
PHAGE T4	022	GILPQRST
PHAGE T5	026	DLNPQ
ARCHAEBACTERIA	030-109	
HALOBACTERIUM CUT.	038	AGHNQRSTVVVX
HALOFERAX VOLCANII	050	AAACDEEFGGGGHIIKKLLLLLMNPPP QRRRSSSTTVVWXY
HALOCOCCUS MORRHUA	054	X
METHANOBAC. THERM.	062	GN
SULFOLOBUS ACIDO.	082	X
THERMOPLASMA ACIDO	090	MX
EUBACTERIA	110-239	
MYCOPLASMA CAPRIC.	114	ACDEFGHIIKKLLLMNPQRRSSTTVWWXY
MYCOPLASMA MYCOID.	118	AGIPSTVX
SPIROPLASMA CITRI	125	WW
STREPTOMYCES GRIS.	130	X
STREPTOMYCES COEL.	131	G
STAPHYLOCOC. EPID.	138	GG
MYCOBAC. SMEG.	142	X
BACILLUS STEARO.	146	FLVY
BACILLUS SUBTILIS	154	AFGIKKLMPRSSSTVWXYY
THERMUS THERMOPHI.	158	DFIMXX
E.COLI	166	AAACDEEFGGGHIIIKLLLMNQQ RRRRRSSSSSTTVVVWXXYYZ
SALMONELLA TYPHI.	170	GGHLPPP
AZOSPIRILLUM LIPO.	172	N
RHODOSPIRIL. RUB.	202	FL
AGMENELLUM QUADR.	206	F
ANACYSTIS NIDULANS	210	LLX
SYNECHOCYSTIS SP.	214	E
ORGANELLES		
CHLOROPLASTS	240-359	
CHLAMYDOMONAS REIN	244	E
EUGLENA GRACILIS	252	P
CODIUM FRAGILE	253	GKMR
SCENEDESMUS OBLIQ.	256	MXY
LUPINUS ALBUS	263	Y
HORDEUM VULGARE	264	DDEQ
TRITICUM AESTIVUM	268	E
ZEA MAYS	272	I
GLYCINE MAX	284	LLL
NICOTIANA TABACUM	292	W
PHASEOLUS VULGARIS	316	FLLLWX
SPINACIA OLERACEA	328	FIILMPTVWX
MITOCHONDRIA	360-599	
SINGLE CELL ORGANISMS AND FUNGI	360-419	
TETRAHYMENA PYRIF.	380	FY
TETRAHYMENA THERM.	384	W
NEUROSPORA CRASSA	392	ALLTVWXY
SACCHAROMYCES CER.	400	FGHIKLMPRRSSSTWXY
PLANTS	420-459	
SOLANUM TUBEROSUM	431	IIL
OENOTHERA SP.	436	F
PHASEOLUS VULGARIS	440	FLLLLMFWXY
ANIMALS	460-599	
ASCARIS SUUM	464	FMS
AEDES ALBOPICTUS	480	DEGHKQRSVX
LOLIGO BLEEKERI	481	KKK
HAMSTER	524	DKRS
RAT LIVER	528	DDFKLLLLRVVW
BOVINE LIVER	536	EGIKLLRSSSTVWXX
HUMAN	588	S
MARSUPIAL	599	D
EUKARYOTIC CYTOPLASM	600-999	
SINGLE CELL ORGANISMS AND FUNGI	600-669	
EUGLENA GRACILIS	604	DF
TETRAHYMENA THERM.	608	QQQX
SCENEDESMUS OBLIQ.	612	FXY
NEUROSPORA CRASSA	620	FX
SACCHAROMYCES CER.	628	ACDEFFGGHHIIKKLLLMNPPRRRSSSTTVVVWXY
SCHIZOSACCHA. POM.	632	EFXY
TORULOPSIS UTILIS	636	AILPVXY
CANDIDA CYLINDRA.	637	LLLSSSSS
PLANTS	670-749	
HORDEUM VULGARE	678	ERF
WHEAT GERM	682	FGIKMRWXYY
BRASSICA NAPUS	686	F
LUPINUS LUTEUS	694	EFGHIMNPSVXY
PHASEOLUS VULGARIS	698	LLLLX
PISUM SATIVUM	702	F
SPINACIA OLERACEA	704	S
NICOTIANA RUSTICA	706	SSSSSYY
SOLANUM TUBEROSUM	707	LW
CUCUMIS SATIVUS	708	L
ANIMALS	750-999	
CAENORHABDI. ELEG.	756	L
ASTERINA AMURENSIS	762	X
BOMBYX MORI	768	AAFFGGI
DROSOPHILA MELANO.	774	EFHKKSSSVVVVXY
EUPHAUSIA SPERBA	786	X
XENOPUS LAEVIS	792	DFX
SALMON LIVER	798	X
CHICKEN	804	W
MOUSE	810	EFFFIKKMQQRRVXZ
RAT	916	DDEKKKLLNNQSSSVVX
RABBIT LIVER	922	DFKKKMV
BOVINE LIVER	928	DFFLLNQRRRTWYZ
CALF LIVER	934	F
COW MAMMARY GLAND	940	LL
SHEEP LIVER	946	HX
HUMAN	999	AAEFGGHLMNNQQSVXYYZ

PART THREE: tRNA and tRNA gene sequences that differ from the conventional alignment

Source	Code	tRNA/tRNA gene
ARCHAEBACTERIA	030-109	
METHANOCOCCUS JAN.	065	Z
MITOCHONDRIA	360-599	
SINGLE CELL ORGANISMS AND FUNGI	360-419	
PHYTOMONAS SP.	367	Q
TRICHOPHYTON MENT.	409	E
ANIMALS	460-599	
LOCUSTA MIGRATORIA	476	S
APIS MELLIFERA	482	T
DAPHNIA PULEX	483	C
DROSOPHILA MELANO.	484	P
PROTOPTERUS DOLLOI	499	S
BALAENOPTERA PHYS.	534	NSS
BALAENOPTERA MUSC.	535	S
HALICHOERUS GRYPUS	537	K
PHOCA VITULINA	538	S
SIAMANG	542	S
RHINOCEROS UNICORN	544	SS
SCELOPORUS OCCID.	545	ACS
STRUTHIO CAMELUS	550	AST
ERINACEUS EUROP.	555	SS
MACACA THIBETANA	559	S
PAPIO HAMADRYAS	567	S
CHIMPANZEE	572	S
PYGMY CHIMPANZEE	573	S
GORILLA	580	S
ORANG UTAN	584	S
HUMAN	588	N

Table 2. Format of tRNA sequences in the databank

PART ONE: SEQUENCES OF tRNA-GENES

```
                                    accept   D-domain          anticodon domain   variable region          T-domain          accep
                                    stem                                          extra loop                                 stem
Number                              012345678911111111111222222222223333333333444444eeeeeeeeeeeeeeeeee44445555555555666666666677777777
                                                012345677890001234567890123456789012345111111112345222222267890123456789012345678901234567890123456
       Anticodon
          Organism          Kingdom
DA0260 TGC PHAGE T5          VIRUS   -GGGCGAATAGTGTCAGC-GGG--AGCACACCAGACTTGCAATCTGGTA----------------G-GGAGGGTTCGAGTCCCTCTTTGTCCACCA
+                                     ==*=*== ===*          *=========      ======                      =====      ========*=*==
DA0340 TGC ARCHAEGLOBUS FULG. ARCHAE -GGGCTCGTAGCTCAGC--GGG--AGAGCGCCGCCTTTGCGAGGCGGAG----------------GCCGCGGGTTCAAATCCCGCCGAGTCCA---
+                                     ==*=====  ====          ====  =====      =====                      =====      =========*==
DA0380 TGC HALOBACTERIUM CUT. ARCHAE -GGGCCCATAGCTCAGT--GGT--AGAGTGCCTCCTTTGCAAGGAGGAT----------------GCCCTGGGTTCGAATCCCAGTGGGTCCA---
+                                     ==*=====  *===          ===*  =====      =====                      =====      ==========*==
DA0420 TGC HALOBACTERIUM HAL. ARCHAE -GGGCCCATAGCTCAGT--GGT--AGAGTGCCTCCTTTGCAAGGAGGAT----------------GCCCTGGGTTGGAATCCCAGTGGGTCCA---
+                                     ==*=====  *===          ===*  =====      =====                      =====      ==========*==
DA0580 TGC METHANOBAC.FORMI. ARCHAE -GGGCCCGTAGCTCAGACTGGG--AGAGCGCCGCCCTTGCAAGGCGGAG----------------GCCCCGGGTTCAAATCCCGGTGGGTCCA---
+                                     ==*====*  ====          ====  =====      =====                      =====      ======*===*==
DA0620 TGC METHANOBAC.THERM. ARCHAE -GGGCCCGTAGCTCAGACTGGG--AGAGCGCCGCCCTTGCAAGGCGGAG----------------GCCCCGGGTTCAAATCCCGGTGGGTCCA---
+                                     ==*====*  ====          ====  =====      =====                      =====      ======*===*==
DA0650 TGC METHANOCOCCUS JAN. ARCHAE -GGGCCCGTAGCTCAGCT-GGG--AGAGCGCCGGCCTTGCAAGCCGGAG----------------GCCGTGGGTTCAAATCCCACCGGGTCCA---
+                                     ==*=====  ====          ====  =====      =====                      =====      ==========*==
DA0651 GGC METHANOCOCCUS JAN. ARCHAE -GGGCTGGTAGCTCAGACTGGG--AGAGCGCCGCATTGGCTGTGCGGAG----------------GCCGCGGGTTCAAATCCCGCCCAGTCCA---
+                                     ==*=====  ====          ====  =====      =====                      =====      ==========*==
DA0660 TGC METHANOCOC.VANI.  ARCHAE -GGGCCCGTAGCTCAGTT-GGG--AGAGCGCTGCCCTTGCAAGGCAGAG----------------GCCGTGGGTTCAAATCCCGCCGGGTCCA---
+                                     ==*=====  ====          ====  =====      =====                      =====      ==========*==
DA0670 TGC METHANOTHRIX SOEH. ARCHAE -GGGCTTGTAGCTCAGCT-GGT--AGAGCGCCGCCTTTGCAAGGCGGAG----------------GCCCTGGGTCCGAATCCCAGCAAGTCCA---
+                                     ==*=====  ====          ====  =====      =====                      =====      ==========*==
DA0680 TGC METHANOTHERM. FER. ARCHAE -GGGCCCATAGCTCAGCCTGGG--AGAGCGCCGCCCTTGCAAGGCGGAG----------------GCCCCGGGTTCAAATCCCGGTGGGTCCA---
+                                     ==*=====  ====          ====  =====      =====                      =====      ==========*==
DA0780 TGC METHANOSPIR. HUNG. ARCHAE -GGGCTCGTAGCTCAGCT-GGA--AGAGCGCGGCGTTTGCAACGCCGAG----------------GCCTGGGGTTCAAATCCCCACGGGTCCA---
+                                     ==*=*==  ====          ====  =====      =====                      =====      ========*=*==
DA0940 TGC THERMOCOCCUS CELER ARCHAE -GGGCCGGTAGCTCAGCCTGGG--AGAGCGTCGGCTTTGCAAGCCGAAG----------------GCCCCGGGTTCGAATCCCGGCCGGTCCACCA
+                                     ==*=====  ====          ====  =====      =====                      =====      ==========*==
DA0980 TGC THERMOPROT. TENAX ARCHAE -GGGCCGGTAGTCTAGC--GGA--AGGACGCCCGCCTTGCGCGCGGGAG----------------ATCCCGGGTTCGAATCCCGGCCGGTCCA---
+                                     ==*=====  ===*          *===  =====      =====                      =====      ==========*==
DA0981 CGC THERMOPROT. TENAX ARCHAE -GGGCCGGTAGTCTAGC--GGA--AGGACGCCCGCCTCGCGCGCGGGAG----------------ATCCCGGGTTCGAATCCCGGCCGGTCCA---
+                                     ==*=====  ===*          *===  =====      =====                      =====      ==========*==
DA1110 TGC BARTONELLA ELIZAB. EUBACT -GGGGCCGTAGCTCAGCT-GGG--AGAGCACCTGCTTTGCAAGCAGGGG----------------GTCGTCGGTTCGATCCCGTCCGGCTCCACCA
+                                     ==*=====  ====          ====  =====      =====                      =   ===      ===  =====*==
DA1130 TGC BARTONELLA QUINT. EUBACT -GGGGCCGTAGCTCAGCT-GGG--AGAGCACCTGCTTTGCAAGCAGGGG----------------GTCGTCGGTTCGATCCCGTCCGGCTCCACCA
+                                     ==*=====  ====          ====  =====      =====                      =   ===      ===  =====*==
```

(Continued in the databank. See text for instructions.)

RESULTS

Presentation of sequences

The sequences in the database are divided into three parts. The first two parts contain the sequences of the tRNA genes and tRNAs, respectively, which can be fitted into the canonical tRNA alignment. The third part lists tRNA and tRNA gene sequences, mainly of animal mitochondria, whose secondary structures differ from most tRNAs and could not be aligned according to Figure 1.

An example for sequence presentation in the database is given in Table 2. Each sequence in the compilation occupies two consecutive lines. The first line begins with the letter 'D' or 'R' and contains the six-position identification code of the sequence ('D' or 'R' for DNA or RNA, respectively; a one-letter code for the amino acid, X for methionine-initiator, Z for selenocysteine; and the four-digit code specifying the organism and isoacceptor. After this, the sequence of the anticodon (in the case of tRNA sequences in its modified form) is given, followed by the name and the kingdom of organism (Table 1), and the sequence (99 standard positions). The second line begins with the sign '+' and contains the information about base-pairing (double helical regions only, tertiary interactions are not annotated). All other lines in the compilation begin with signs other than 'D,' 'R' or '+' (usually '*') and contain comments.

Nucleotides involved in Watson–Crick pairs are marked with '=', the GU pairs are indicated with the sign '*'. Nucleotides 26 and 44 are considered to form a base-pair included in the anticodon stem (Fig. 1).

The sequences in orginal publications denoted as 'yeast' are assigned to *Saccharomyces cerevisiae*. The user should be aware, however, that some of these organisms have possibly been misclassified and that the original literature should be consulted.

This compilation uses a one-letter code for all nucleotides including modified ones. For standard nucleotides, adenosine, cytidine, guanosine, thymidine and uridine the usual abbreviations, A, C, G, T and U, respectively, are used. To designate modified nucleotides, the other ASCII signs are employed as defined in Table 3. Terminology and structure of the modified nucleosides occurring in tRNAs were used according to refs 2 and 3. Positions in particular sequence which are not filled (gaps in the generalised structure, Fig. 1) are indicated by a dash. All nucleotide insertions are denoted by underlining at the place of insertion.

Numbering and alignment of the variable region

The alignment of the variable region has been done in accordance with Steinberg and Kisselev (4). The extra arm is placed between nucleotides 45 and 46. It includes two double helical strands forming a stem and a loop. The annotations of the nucleotides in the extra arm positions begin with the letter 'e' (extra) followed by a one- or two-digit number. We have reserved a space for 7 bp in the stem and 5 nt in the loop. The nucleotides in the loop are numbered from 1 to 5, whereas the nucleotides in the stem are numbered from 11 to 17 (5′-branch) and from 27 to 21, in the reverse order, (3′-branch), to indicate base-pair formation between nucleotides 11–21, 12–22, etc. (Fig. 1). In the tRNAs where the extra arm position 45 is empty but where the nucleotides 46–48 between the extra arm and T-domain are present, the positions will be filled in the order 48, 46,

Table 3. Modified nucleosides in tRNA and their abbreviations

One-letter code of nucleotides	Symbol [2,3]	Name [2,3]
U	U	uridine
C	C	cytidine
A	A	adenosine
G	G	guanosine
T	T	thymine (for sequences of tRNA genes only)
-		empty position
_	(underline)	insertion (see footnote for further information)
.		unknown nucleotide
H	?A	unknown modified adenosine
"	m1A	1-methyladenosine
/	m2A	2-methyladenosine
+	i6A	N^6-isopentenyladenosine
*	ms2i6A	2-methylthio-N^6-isopentenyladenosine
=	m6A	N^6-methyladenosine
6	t6A	N^6-threonylcarbamoyladenosine
B	m6t6A	N^6-methyl-N^6-threonylcarbamoyladenosine
[	ms2t6A	2-methylthio-N^6-threonylcarbamoyladenosine
:	Am	2'-O-methyladenosine
I	I	inosine
O	m1I	1-methylinosine
^	Ar(p)	2'-O-(5-phospho)ribosyladenosine
'	io6A	N^6-(cis-hydroxyisopentenyl)adenosine
<	?C	unknown modified cytidine
%	s2C	2-thiocytidine
B	Cm	2'-O-methylcytidine
M	ac4C	N^4-acetylcytidine
?	m5C	5-methylcytidine
'	m3C	3-methylcytidine
}	k2C	lysidine
>	f5C	5-formylcytidin
°	f5Cm	2'-O-methyl-5-formylcytidin
;	?G	unknown modified guanosine
S	Gr(p)	2'-O-(5-phospho)ribosylguanosine
K	m1G	1-methylguanosine
L	m2G	N^2-methylguanosine
#	Gm	2'-O-methylguanosine
R	m22G	N^2,N^2-dimethylguanosine
|	m22Gm	N^2,N^2,2'-O-trimethylguanosine
7	m7G	7-methylguanosine
(	fa7d7G	archaeosine
Q	Q	queuosine
8	manQ	mannosyl-queuosine
9	galQ	galactosyl-queuosine
Y	yW	wybutosine
W	o2yW	peroxywybutosine
N	?U	unknown modified uridine
{	mnm5U	5-methylaminomethyluridine
2	s2U	2-thiouridine
J	Um	2'-O-methyluridine
4	s4U	4-thiouridine
&	ncm5U	5-carbamoylmethyluridine
1	mcm5U	5-methoxycarbonylmethyluridine
S	mnm5s2U	5-methylaminomethyl-2-thiouridine
3	mcm5s2U	5-methoxycarbonylmethyl-2-thiouridine
V	cmo5U	uridine 5-oxyacetic acid
5	mo5U	5-methoxyuridine
I	cmnm5U	5-carboxymethylaminomethyluridine
$	cmnm5s2U	5-carboxymethylaminomethyl-2-thiouridine
X	acp3U	3-(3-amino-3-carboxypropyl)uridine
,	mchm5U	5-(carboxyhydroxymethyl)uridinemethyl ester
)	cmnm5Um	5-carboxymethylaminomethyl-2'-O-methyluridine
~	ncm5Um	5-carbamoylmethyl-2'-O-methyluridine
D	D	dihydrouridine
P	Ψ	pseudouridine
]	m1Ψ	1-methylpseudouridine
Z	Ψm	2'-O-methylpseudouridine
T	m5U	ribosylthymine
F	m5s2U	5-methyl-2-thiouridine
\	m5Um	5, 2'-O-dimethyluridine

47, i.e., tRNAs use position 48, 46 and 47 for the first, second and third nucleotide, respectively, depending on the length of the sequence in this region. A similar situation occurs in tRNAs without a long extra arm, where the most variable position 47 is deleted in many sequences.

Alignment of animal mitochondrial tRNAs

In properly aligned tRNA sequences, nucleotides occupying the same position in different tRNA sequences should play a comparable structural or functional role. Most animal mitochondrial tRNAs cannot be easily aligned with other tRNAs mainly because of the absence of information on their three-dimensional structure. Experimental data, however, point to the existence of tertiary interactions in these tRNAs. In this compilation, we use an alignment which accounts for these interactions as much as possible. Where we could do so, the animal mitochondrial tRNAs were included in Parts I and II. The alignment of animal mitochondrial tRNA is, however, not yet unambiguous.

Some animal mitochondrial tRNAs have completely unusual secondary structure and cannot be fitted in the tRNA alignment used here (Parts I and II). We treated these sequences separately including them into Part III. Here, each particular sequence has its own alignment. To this group belong the tRNAs from: (i) mitochondria of a parasitic worm lacking the T- or D-domain, (ii) mitochondria of mollusks, insects and echinoderm, with extended anticodon and T-stems and (iii) mammalian mitochondria, lacking the D-domain.

For some tRNA genes the secondary structure pattern cannot be clearly established. We have also included these sequences in Part III. It is possible that posttranscriptional modifications of these tRNAs will result in improvement of the secondary structure.

ACKNOWLEDGEMENT

This project was supported by Fonds der Chemischen Industrie, Deutsche Forschungsgemeinschaft, Project Sp 243/5-1.

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